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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,955	02/28/2001	Rold W. Von Borstel	1331-334	3848

7590 09/09/2004

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EXAMINER

LEWIS, PATRICK T

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/763,955

Applicant(s)

VON BORSTEL, RELD W.

Examiner

Patrick T. Lewis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on April 21-22, 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48-69 is/are pending in the application.
- 4a) Of the above claim(s) 60, 61 and 69 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 48-59 and 62-68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>04212004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 19 dated July 21, 2003 is acknowledged.
2. Claims 60-61 and 69 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 19 dated July 21, 2003.

Applicant's Responses Dated April 21-22, 2004

3. In the Responses filed April 21-22, 2004, claims 48-56 were amended.
4. Claims 48-69 are pending. Claims 60-61 and 69 are drawn to a nonelected invention. An action on the merits of claims 48-59 and 62-68 is contained herein below.
5. The provisional rejection of claims 48-53 and 62 under 35 U.S.C. 101 as claiming the same invention as that of claims 22, 24, 26, 28-30, and 14 of copending Application No. 09/930,494 has been withdrawn in view of applicant's amendments filed April 21-22, 2004.
6. The provisional rejection of claims 54-59 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31-32 and 38-41 of copending Application No. 09/930,494 is maintained for the reasons of record as set forth in the Office Action dated October 22, 2003.

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7. The objection to claims 48, 56, and 62 has been rendered moot in view of applicant's amendments dated April 21-22, 2004.

8. The rejection of claims 48-59 and 62-68 under 35 U.S.C. 112, first paragraph, has been rendered moot in view of applicant's amendments dated April 21-22, 2004.

9. The rejection of claims 48-59 under 35 U.S.C. 112, second paragraph, is maintained for the reasons of record set forth in the Office Action dated October 22, 2003.

10. The rejection of claims 48-59 and 62-68 under 35 U.S.C. 103(a) is maintained for the reasons of record set forth in the Office Action dated October 22, 2003.

Objections/Rejections of Record Set Forth in Office Action

Dated October 22, 2003.

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. Claims 54-59 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31-32 and 38-41 of copending Application No. 09/930,494. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 54-55 and the invention of the '494 application differ in scope with regards to the conditions being treated or prevented; however, the claims of the

'494 application and the instant invention overlap substantially, and to issue a patent to the claims of the instant application could extend the patent term for subject matter the '494 application.

Claims 56-59 differ from the invention of the '494 application in that the invention of the '494 application is limited to treatment (does not read on prevention); however, the methodological steps and active agents employed by both methods are the same.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Applicant has failed to set forth arguments as to why the provisional rejection is improper.

14. Claims 48-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "a pyrimidine nucleotide precursor" renders all claims in which the phrase appears indefinite. In the absence of distinct chemical core, distinct language to describe the structural modifications, or the chemical names of precursor compounds of this invention, the identity of said precursors would be difficult to describe and the metes and bounds of said precursor compounds applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

15. Applicant's arguments filed April 21-22, 2004 have been fully considered but they are not persuasive. Applicant argues that one of ordinary skill in the art

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would have no difficulty in understanding said phrase as used in the instant claims.

The examiner respectfully disagrees. The primary purpose of the requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. If the scope of the invention sought to be patented cannot be determined from the language of the claims with a reasonable degree of certainty, a rejection of the claims under 35 U.S.C. 112, second paragraph is appropriate. The citations in the specification wherein applicant alleges the term is defined have also been noted. Although it is proper to use the specification to interpret what is meant by a word or phrase in a claim, this is not to be confused with adding an extraneous limitation appearing in but not required by the specification, which is improper.

16. Claims 48-59 and 62-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Page et al. Proc. Natl. Acad. Sci. USA, 1997, Vol. 94, pages 11601-11606 (Page) in combination with von Borstel et al. U.S. Patent 6,316,426 B1 (von Borstel).

Claims 48 and 62 are drawn to a method for treating a congenital mitochondrial disease comprising administering an effective amount of a pyrimidine nucleoside precursor. Claims 49 and 63 are drawn to a method for treating Alzheimer's disease comprising administering an effective amount of a pyrimidine nucleoside precursor. Claims 50 and 64 are drawn to a method for treating Huntington's disease comprising administering an effective amount of a

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pyrimidine nucleoside precursor. Claims 51-52 and 65 are drawn to a method for treating a neuromuscular degenerative disease comprising administering an effective amount of a pyrimidine nucleoside precursor. Claims 53-59 and 66-68 are drawn to a method for treating a neuromuscular degenerative disease comprising administering an effective amount of a pyrimidine nucleoside precursor.

Page teaches the treatment of patients described with a syndrome that included developmental delay, seizures, ataxia, recurrent infections, severe language deficit, and an unusual behavioral phenotype characterized by hyperactivity, short attention span, and poor social interaction (Abstract). Patients were treated with 50-1,000 mg/kg per day (page 11604, column 2).

Page differs from the instantly claimed invention in that Page does not teach the use of acyl derivatives of uridine nor does Page explicitly teach all the conditions within the scope of the instantly claimed invention. However, these deficiencies would have been obvious to one of ordinary skill in the art at the time of the invention when viewed in combination with von Borstel.

von Borstel teaches a family of uridine and cytidine derivatives for the treatment of a variety of disorders including heart, muscle, plasma, liver, bone, diabetic, and neurological conditions (column 8, lines 20-24). The acyl derivatives of uridine comprise compounds having the formula (II) wherein R is an acyl radical of an unbranched fatty acid, an amino acid, a dicarboxylic acid, or a carboxylic acid selected from one or more of the group consisting of glycolic acid, pyruvic acid, orotic acid, and creatine (column 9, lines 1-23). 2',3'5'-tri-O-

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acetyl uridine is taught as being a preferred active agent (column 10, lines 2-5).

The invention contemplates the use of these acyl derivatives for treating a variety of physiological and pathological conditions, including treatment of cardiac insufficiency and myocardial infarction, treatment of liver disease or damage, muscle performance, treatment of lung disorders, diabetes, central nervous system disorders such as cerebrovascular disorders, Parkinson's disease, and senile demetias (column 10, lines 24-35).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat patients having a mitochondrial disease with an acylated derivative of uridine as taught by the prior art. The examiner recognizes that all of the conditions listed as being treatable/preventable by the instant uridine compounds are not explicitly embraced by the prior art; however, applicant has merely found a new property of the instant uridine compounds and such a discovery does not constitute a new use. In the instant case, the population to be treated is a subject having a mitochondrial disease. The prior art teaches the treatment of this population with an acylated derivative of uridine rendering the instantly claimed method *prima facie* obvious.

17. Applicant's arguments filed April 21-22, 2004 have been fully considered but they are not persuasive. Applicant argues that the finding by Page that nucleotide precursors (ribose and uridine) are clinically useful in treating a disorder in which the only known molecular deficit is an excess on an enzyme involved in nucleotide degradation, would not have led one of ordinary skill to suspect that uridine or ribose would be used in treating conditions caused by

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mitochondrial respiratory chain dysfunction, even those which might manifest some similar symptoms. Applicant further argues that von Borstel does not cure the deficiencies of Page.

The examiner respectfully disagrees. As set forth supra, von Borstel teaches a family of uridine and cytidine derivatives for the treatment of a variety of disorders including heart, muscle, plasma, liver, bone, diabetic, and neurological conditions (columns 1-2; column 8, lines 20-24). Von Borstel further teaches that mitochondrial dysfunction contributes to various disease states. Von Borstel teaches uridine and cytidine derivatives which compensate broadly for mitochondrial deficits involving a wide variety of molecular pathologies, since, in many cases, precise diagnosis of molecular lesions in mitochondrial disorders are difficult. Von Borstel teaches a practical treatment of mitochondrial diseases that is beneficial in the case of mitochondrial electron transport chain deficits regardless of the specific molecular defects. Examples of conditions that are treated with the uridine and cytidine derivatives include neuromuscular and neurodevelopmental disorders that appear in childhood, common age-related degenerative diseases like Alzheimer's or Parkinson's Diseases, epilepsy, and migraines.

Applicant's arguments are not convincing in view of that which the prior art teaches as a whole. In the absence of some proof of a secondary nature to obviate the rejection as set forth in the Office Action dated October 22, 2003, or of some specific limitations which would tip the scale of patentability in the favor of the instantly claimed invention, it would have been obvious to one of ordinary

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skill in this art at the time of the invention to treat mitochondrial diseases with a pyrimidine nucleotide precursor as applicant has done with the above cited references before them.

Conclusion

18. Claims 48-69 are pending. Claims 60-61 and 69 are drawn to a nonelected invention. Claims 48-59 and 62-68 are rejected. No claims are allowed.

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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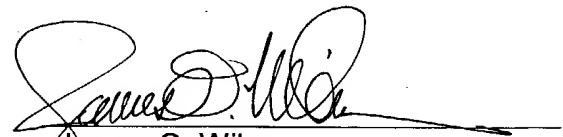
Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623



James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

ptl
August 26, 2004